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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,530	02/01/2007	Sergei Gryaznov	074/002	5144

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,530	GRYAZNOV ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-80* is/are pending in the application.

4a) Of the above claim(s) *52-56 and 65-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-51,57-64 and 75-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12-14-06, 2-27-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 8-21-09.

Claims 42-80 are pending in the instant application.

Election/Restrictions

Applicant's election with traverse of Group I, claims 42-46, 57-64, 78-80, and HIV as the target gene, in the reply filed on 8-21-09 is acknowledged. The traversal is on the ground(s) that restriction is improper because all of the members of the claims possess the common property of possessing a ribo-N3' -> P5' phosphoramidate or thiophosphoramidate linkage, and that no serious burden would be made for the examination of the different target genes also claimed in addition to HIV Applicant also argues that claim 42 is a linking claim and, if found allowable, would require rejoinder of the other claims. Applicant additionally argues that, upon determination of allowability of the composition claims, the methods claims that are drawn to the same scope as the allowable composition claims are also to be rejoined and examined on their merits. This is not found fully persuasive because the proper examination required for all of the target genes claimed would pose a serious burden on the examiner because of the myriad of data bases required to search, which include but are not limited to searching the non-patent, patent, and relevant sequence data bases. In addition, the siRNA, while sharing the common property of possessing a ribo-N3' -> P5' phosphoramidate or thiophosphoramidate linkage, are functionally, structurally, biologically and chemically different and distinct because they target different sequences and so comprise different

sequences, and the ability of one siRNA to inhibit its corresponding target gene does not necessarily predict the ability of a different and distinct siRNA to inhibit its corresponding target gene or target sequence. Applicant is correct that, upon indication of allowability, the methods claims are to be rejoined with the composition claims (of identical scope) and examined on their merits.

The requirement is still deemed proper and is therefore made FINAL.

Claims 52-56, 65-74 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Claims 42-51, 57-64, 75-80 have been rejoined and examined on their merits as set forth below. Applicant timely traversed the restriction (election) requirement in the reply filed on 8-21-09.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 42-48, 50, 51, 57-64, 75-80 are rejected under 35 U.S.C. 102(e) as being anticipated by Manoharan et al (US 2005/0164235).

Manoharan et al (US 2005/0164235) teach iRNA molecules, including single or double stranded siRNA molecules between 15-25 nucleobases in length comprising at least one, or optionally all ribo-N3' -> P5' phosphoramidate or thiophosphoramidate linkages, which iRNA has a lipid moiety covalently conjugated to its 5' or 3' terminus, which lipid moiety is optionally a fatty acid, hydrocarbon or sterol, and which iRNA targets and inhibits the expression of a human endogenous target gene or a HIV gene (see esp. pages 5, 6, 8-11, 22, 23, 35-37, 40, 42, 49, 53-54).

Claims 42-44, 57, 59, 60, 61, 78-80 are rejected under 35 U.S.C. 102(e) as being anticipated by Davis (US 2005/0136430).

Davis (US 2005/0136430) teach iRNA molecules, including single or double stranded siRNA molecules between 15-25 nucleobases in length comprising at least one, or optionally all ribo-N3' -> P5' phosphoramidate or thiophosphoramidate linkages, and which iRNA targets and inhibits the expression of a human endogenous target gene (see esp. the abstract, pages 3, 5-8, 14-16).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 42-51, 57-64, 75-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Manoharan et al (US 2005/0164235) and Davis (US 2005/0136430), the combination in view of Jiang et al (US 2006/0116331).

The claims are drawn to iRNA molecules, including single and double stranded siRNA molecules between 15-25 nucleobases in length comprising at least one, or optionally all ribo-N3' -> P5' phosphoramidate or thiophosphoramidate linkages, which iRNA has a lipid moiety covalently conjugated to its 5' or 3' terminus, which lipid moiety is optionally a fatty acid, hydrocarbon or sterol, which fatty acid is optionally substituted with a fluorine, and which iRNA targets and inhibits the expression of a human endogenous target gene or a HIV gene

Manoharan et al (US 2005/0164235) teach iRNA molecules, including single or double stranded siRNA molecules between 15-25 nucleobases in length comprising at least one, or optionally all ribo-N3' -> P5' phosphoramidate or thiophosphoramidate linkages, which iRNA has a lipid moiety covalently conjugated to its 5' or 3' terminus,

which lipid moiety is optionally a fatty acid, hydrocarbon or sterol, and which iRNA targets and inhibits the expression of a human endogenous target gene or a HIV gene (see esp. pages 5, 6, 8-11, 22, 23, 35-37, 40, 42, 49, 53-54).

Davis (US 2005/0136430) teach iRNA molecules, including single or double stranded siRNA molecules between 15-25 nucleobases in length comprising at least one, or optionally all ribo-N3' -> P5' phosphoramidate or thiophosphoramidate linkages, and which iRNA targets and inhibits the expression of a human endogenous target gene (see esp. the abstract, pages 3, 5-8, 14-16).

The primary references of Manoharan and Davis do not teach fatty acids substituted with at least one fluorine.

Jiang et al (US 2006/0116331) teach oligonucleotides with covalently conjugated lipid moieties, which lipids comprise fatty acids comprising at least one fluorine, and Jiang teaches the advantages of incorporating fluorines into fatty acids and conjugating them to oligonucleotides for enhancing amphiphilic molecules in their anti-HIV activity (see esp. paragraphs 0023-0035).

It would have been obvious to incorporate fluorines into fatty acids of lipid groups that are covalently linked to inhibitory oligonucleotides, including single and double stranded iRNA molecules because Jiang taught the methods to do this, and it was well known in the art that fluorocarbon group analogs have enhanced anti-HIV capabilities. One would have been motivated to design these fluorine containing inhibitory molecules as a means of enhancing the therapeutic efficacy of iRNA molecules that target HIV in subjects in need of such therapy. One would have reasonably expected that the

lipophilicity of inhibitory oligonucleotides would be enhanced by the conjugation of these fatty acid containing lipid moieties, enhancing cellular penetration, and that these oligonucleotides would provide better anti-HIV therapeutic effects because of enhanced cellular uptake and because of their cumulative anti-HIV and HIV inhibitory capacities.

For these reasons, the instant invention would have been obvious to one of skill in the art at the time of filing.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 42-51, 57-64, 75-80 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 7494982, in view of Gryaznov et al (US 2005/0113325). Although the conflicting claims are not identical, they are not patentably distinct from each other

because both sets of claims are drawn to molecules comprising at least one ribo-N3' -> P5' phosphoramidate or thiophosphoramidate linkage.

Gryaznov et al (US 2005/0113325) teach iRNA molecules, including single and double stranded siRNA molecules between 15-25 nucleobases in length comprising at least one, or optionally all ribo-N3' -> P5' phosphoramidate or thiophosphoramidate linkages, which iRNA has a lipid moiety covalently conjugated to its 5' or 3' terminus, which lipid moiety is optionally a fatty acid, hydrocarbon or sterol, which fatty acid is optionally substituted with a fluorine, and which iRNA targets and inhibits the expression of a human endogenous target gene (see entire document, including claims 1-25).

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jane Zara whose telephone number is (571) 272-0765. If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, Tracy Vivlemore, can be reached on (571) 272-2914. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
12-18-09

/Jane Zara/

Primary Examiner, Art Unit 1635